Hemorrhagic Fever with Renal Syndrome

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Abstract

Hemorrhagic fever with renal syndrome (HFRS) is caused by the Hantaviruses, a group enveloped RNA viruses transmitted through contact with infected rodent urine or feces. Although distributed widely through Europe, Asia, and the New World, infections acquired in Korea, China, and Russia tend to be among the most severe. The initial presentation of HFRS is extremely variable, but generally includes fever, malaise, headache and abdominal pain. Laboratory findings that may lead to the diagnosis include thrombocytopenia, azotemia, elevated serum creatinine, or proteinuria. We present the case of a patient that acquired hemorrhagic fever with renal syndrome in South Korea.

Introduction

During the Korean War, United Nations troops were affected by an acute febrile illness associated with renal failure, thrombocytopenia, and hemorrhages; similar illnesses had been described in Chinese medical writings as early as 960 AD. During the Korean War, researchers were able to demonstrate the infective nature of the illness and suspected a rodent vector, but the etiologic agent remained obscure. [1] The disease is now known as hemorrhagic fever with renal syndrome and is known to be caused by the Hantaviruses, a family of enveloped RNA viruses. Transmission occurs through inhalation of aerosolized rodent excreta and symptoms begin 1-5 weeks after exposure.

Case Report

A 19-year-old previously healthy woman serving in the US Army was stationed in Korea and went to conduct field-training exercises with her unit. During the exercises, the patient spent most of her time riding in vehicles and slept in an old wooden barracks at night. No signs of rodent inhabitation were noted during her stay. On the tenth day of the exercise, she began to experience an intense headache and blurry vision. Over the next several days, her symptoms expanded to include fever, fatigue, abdominal pain, and myalgias. She sought medical care numerous times and was diagnosed as having migraines, dehydration, or a viral syndrome.

Fourteen days after the start of the field exercises, she was admitted to the hospital after developing acute renal failure. On admission, she was febrile to 101.3°F and was noted to have periorbital and extremity edema; platelets were 79 x 10^9/L, serum creatinine was 1.3 mg/dL, and urine dipstick showed 3+ proteinuria. The patient remained in Korea until her creatinine rose to 4.9 mg/dL, at which time she was transferred to Tripler Army Medical Center in Hawaii. Shortly before transfer, serology returned positive for Hantaan virus IgM and the patient was started on IV ribavirin. On arrival at Tripler, the patient's platelet count was 257 x 10^9/L, her serum creatinine remained 4.9 mg/dL, and she continued to appear edematous. IV ribavirin was discontinued and the patient underwent a brisk auto-diuresis. She recovered uneventfully with only supportive care and was discharged from the hospital twenty-two days after her field exercise began. Her serum creatinine was 1.2 mg/dL on discharge.

Discussion

Approximately 150,000 people are hospitalized each year due to clinical illness from Hantavirus infection, predominately in Korea, China, and Eastern Russia. The case-mortality ratio for HFRS in this region is approximately 5-10%. When suspected clinically, the diagnosis of HFRS is confirmed with serology. A positive IgM or a four-fold rise in Hantavirus IgG titer confirms Hantavirus infection.

HFRS is classically divided into five sequential but overlapping phases: Febrile, hypotensive, oliguric, diuretic, and convalescent. During the initial febrile phase, patients with HRFS typically present with abrupt onset of fever and chills, lethargy, and weakness, which may later be accompanied by dizziness, thirst, anorexia, myalgias, and abdominal pain. Physical exam may initially be notable for conjunctival injection or pharyngeal erythema. Laboratory studies are usually normal at this point. Then patients progress into the hypotensive phase. In addition to a drop in blood pressure, patients' platelet counts and renal function decrease and proteinuria develops. Some patients may progress to shock. The disease then progresses to the oliguric phase, characterized by difficulties regulating electrolytes and volume status, potentially leading to pulmonary edema. Although platelet counts begin to

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recover in the oliguric phase, patients are most prone to hemorrhage at this point, including gastrointestinal or retroperitoneal hemorrhage. The diuretic phase is marked by a return of renal function, but can be complicated by electrolyte abnormalities as fluid shifts occur. During the convalescent phase, renal function continues to improve.[2] An important marker in the course of HFRS is the patient's platelet count; a normalization of the platelet count heralds the return of renal function.[3] In this case, the patient from Korea had a normal platelet count on arrival in Hawaii, which was a very good prognostic indicator.

Major causes of mortality in HFRS are related to shock, electrolyte abnormalities, pulmonary edema and hemorrhage. The underlying pathophysiologic abnormality is thought to be endothelial dysfunction.[4] Treatment is generally supportive: cautious use of IV fluids or pressors for hypotension, hemodialysis if indicated for volume overload, administration of blood products, and treatment of electrolyte disturbances.

Intravenous ribavirin exists as a specific treatment for hemorrhagic fever with renal syndrome, although it is still experimental at the current time. In a study conducted in China, intravenous ribavirin given within six days of the onset of symptoms significantly reduced the mortality associated with HFRS. Most of the benefit of ribavirin appears to be associated with a reduction in the risk of entering the oliguric phase. The only side effect noted with ribavirin was a mild hemolytic anemia, which reversed with cessation of drug therapy.[5] In this case, the patient arrived in Hawaii eight days after the onset of her symptoms and already appeared to be recovering, so the ribavirin was not continued after she was transferred.

Conclusion

The diagnosis of hemorrhagic fever with renal syndrome should be entertained in any patient with a febrile illness and travel to an endemic area, especially if associated with severe malaise, headache, myalgias, or abdominal pain. Common screening laboratory studies, such as a complete blood count, chemistries, or urinalysis, may show thrombocytopenia, renal failure or proteinuria, offering a clue to the diagnosis. Hantavirus serologies can confirm the diagnosis of HFRS. Treatment is generally supportive, but IV ribavirin may be beneficial if initiated early in the course of the disease.

Refrences

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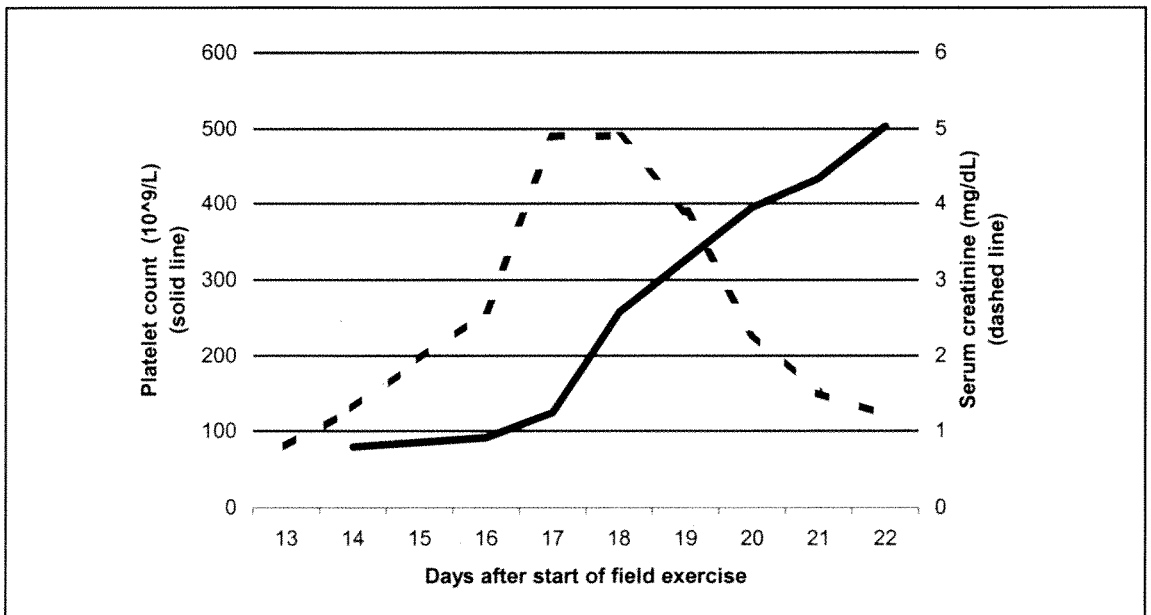

Figure 1.— Serum creatinine and platelet count after start of field exercise